HALEWOOD LABORATORIES PVT. LTD.

BRENALYTE

Combipack containing Oral Rehydration Salts BP 20.5g and Zinc Sulfate Tablets USP 20 mg

PACK STYLE: 2 sachets of ORS + 1 blister containing Zinc Tablets

SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

1. Name of drug product

BRENALYTE

1.1 (Trade) name of product

Combikit containing Oral Rehydration Salts BP and Zinc Sulfate Tablets USP

1.2 Strength

Combikit contains

A. Oral Rehydration Salts BP

Each sachet of 20.5 gm contains

Sodium Chloride BP……2.6 gm

Potassium Chloride BP……1.5 gm

Sodium Citrate BP……2.9 gm

Glucose (Anhydrous) BP……..…13.5 gm

B. Zinc Sulfate Tablets USP

Each uncoated dispersible tablet contains

Zinc Sulfate Monohydrate USP

equivalent to Elemental Zinc 20 mg

Excipients Q.S.

1.3 Pharmaceutical Dosage Form

Powder for oral administration

Tablets for oral administration

2. QUALITATIVE & QUANTITATIVE COMPOSITION

A. Oral Rehydration Salts

2.1 Qualitative Declaration

Each sachet of 20.5 gm contains

Sodium Chloride BP……2.6 gm

Potassium Chloride BP……1.5 gm

Sodium Citrate BP……2.9 gm

Glucose (Anhydrous) BP……..…13.5 gm

2.2 Quantitative Declaration

Batch size: 40,000 pouches

Qualitative and Quantitative Formula for batch (40,000 pouches)

Sr. No.	Ingredient	Grade	Theoretical quantity/sachet	Overages	Theoretical quantity for batch in kg
1	Glucose (Anhydrous)	BP	2.6	Nil	104.000
2	Sodium Chloride	BP	1.5	Nil	60.000
3	Potassium Chloride	BP	2.9	Nil	116.000
4	Sodium Citrate	BP	13.5	Nil	540.000
Total				**---**	**820.000**

B. Zinc Sulfate Tablets USP

2.1 Qualitative Declaration

Each uncoated dispersible tablet contains

Zinc Sulfate Monohydrate USP

equivalent to Elemental Zinc 20 mg

Excipients Q.S.

2.2 Quantitative Declaration

Batch Size: 1200000 Tablets = 686.00 kg

Sr. No.	Ingredient	Grade	Theoretical qty./tablet in mg	Overages	Actual quantity for batch in kg
1.	Zinc Sulphate Monohydrate	USP	54.890	Nil	65.868
2.	Microcrystalline Cellulose (MCCP)	BP	173.000	Nil	207.60
3.	Lactose	BP	122.000	Nil	146.40
4.	Maize Starch	BP	170.910	Nil	205.09
5.	Croscarmellose sodium	BP	10.000	Nil	12.00
6.	PVP K – 30	BP	6.000	Nil	7.200

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7.	Isopropyl Alcohol*	BP	---	Nil	25.00 ltr
8.	Purified Talc	BP	3.000	Nil	3.60
9.	Sodium Starch Glycolate	BP	3.000	Nil	3.60
10.	Aerosil (Colloidal Anhydrous Silica)	BP	0.600	Nil	0.720
11.	Croscarmellose sodium	BP	10.000	Nil	12.00
12.	Kyron T-314 (Polacrillin Potassium)	BP	3.000	Nil	3.60
13.	Flavour Orange	IH	15.000	Nil	18.00
14.	Aspartame	BP	6.600	Nil	7.92
15.	Magnesium Stearate	BP	2.000	Nil	2.40
Total				---	686.00 kg

3. PHARMACEUTICAL DOSAGE FORM

Powder for oral administration

Tablets for oral administration

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

ORS

For the treatment of acute diarrhoea and the treatment and prevention of dehydration by replacing fluids and electrolytes lost through diarrhoea.

ZINC TABLET

Zinc is a trace element that is essential for normal growth and development of infants and children.

Zinc plays an important role in cellular growth of the body and improves the immunity of the body and resistance against infections. The use of zinc tablets along with oral rehydration therapy (ORT) decreases the severity and duration of diarrhoea. Zinc administration during diarrhoea decreases hospital admission rates by 15-20% and child mortality by 3-5%. It can decrease the incidence of subsequent episodes of diarrhoea and possibly also pneumonia over next 3 months.

4.2 Posology and Method of Administration

A. Oral Rehydration Salts

Reconstitution: Only with water and at the volume stated.

Adults and children: The content of sachet should be dissolved in approximately 1000 ml of cool, fresh, clean drinking water. The resulting solution is both clear and colourless.

Infants: The water should be boiled then cooled before reconstitution as above.

The reconstituted cooled solution should be used immediately and the unused remainder discarded, or stored in a refrigerator for no longer than 24 hours. Do not boil after reconstitution. The product must only be used at the recommended dilution.

Dosage: Oral fluid replacement and maintenance therapy must be tailored to individual patient's needs. The volume of solution used will depend on the weight and age of the patient, using the basic principle of firstly rehydrating the patient by replacing lost fluid and thereafter maintaining fluid replacement in line with the volume of fluid lost from stools or vomiting plus normal daily requirements. As a basic guide, a daily intake of 150 ml/kg bodyweight for infants (under 2 years of age) or 20-40ml/kg for adults and children is needed.

Replacement of fluid losses with ORS solution

Infants (under 2 years of age): See special warnings and precautions for use. sachets according to directions and administer at 1-1.5 times usual feed volume. No milk (other than breast milk) or solids should be given during the first 24 hours. In breast-fed infants, ORS should be given before the feed. The re-introduction of normal feeding should only take place when symptoms of diarrhoea are abating and should be added gradually to make up the total daily fluid requirements.

Child 1–11 months: 1–1½times usual feed volume to be given

Child 1–11 years: 200 mL, to be given after every loose motion

Child 12–17 years: 200–400 mL, to be given after every loose motion, dose according to fluid loss

Adult: 200–400 mL, to be given after every loose motion, dose according to fluid loss.

In adults and children ORS can be given in amounts necessary to satisfy thirst. As with infants, solids should be avoided during the first day, but may be gradually resumed as necessary during day 2.

It is extremely difficult to over-hydrate by mouth, thus when there is normal renal function, it is better to give more ORS than less.

B. Zinc Sulfate Tablets

These are dispersible tablets; hence it should be dissolved in a glass of water or any other liquid.

Use in adults

The recommended dose for adults is one tablet, dissolved in water, once daily after meals.

Use in children

The recommended dose for children is as follows: More than 30kg: one tablet, dissolved in water, once daily after meals. 10-30kg: half a tablet, dissolved in water, once daily after meals. Less than 10kg: half a tablet, dissolved in water, once daily after a meal. This should be followed for 10-14 days as required.

4.3 Contraindications

ORS

Hypersensitivity to any of the ingredients.

Oral treatment is inappropriate in such conditions as severe dehydration, which requires parenteral fluid therapy or intestinal obstruction.

It is necessary for medical supervision in the presence of renal disease, including anuria or prolonged oliguaria, severe and persistent diarrhea and vomiting, inability to drink or retain oral fluids.

ZINC TABLET

Hypersensitivity to Zinc or any other of the excipients used.

4.4 Special Warnings and Precautions for Use

ORS

Severe and persistent diarrhoea should be treated under medical supervision. If symptoms persist for more than 24 — 48 hours, medical advice should be sought. Inability to drink or retain fluids requires medical supervision.

Children

• Rehydration treatment should only be given to children under 1 year of age on medical advice.

• If a young child (particularly one under 6 months of age) has diarrhoea and/or vomiting advice should be sought from a pharmacist, doctor or other health care professional. If the diarrhoea and/or vomiting is severe the child should be seen by a doctor as soon as possible.

Renal Impairment

• Medical supervision is necessary in patients with renal disease, including anuria and prolonged oliguria.

Hepatic Impairment : Low potassium or Sodium diets: Diabetes

• Treatment should be supervised by a physician.

This product contains dextrose. Patients with rare-glucose-galactose malabsorption should not take this medicine.

ZINC TABLET

Drugs which may inhibit zinc absorption, such as penicillamine, sodium valproate and ethambutol, should not be co-administered with Zinc Tablets, unless the risks of discontinuation of the drug are judged to outweigh the benefit of zinc in treatment of the child's diarrhoea.

Excipients

Zinc 20mg Tablets contain aspartame, a source of phenylalanine. This should be considered

when prescribing the product to patients with phenylketonuria

4.5 Interaction with Other Drugs, Other Forms of Interactions

ORS

None stated

ZINC TABLET

Antibiotics

When taken together, zinc may reduce the absorption of tetracyclines (but not doxycycline), and

quinolone antibiotics. In addition, zinc may also interfere with the absorption of cephalexin or ceftibuten. An interval of at least three hours should be allowed between administration of zinc and any of these medicines.

4.6 Fertility, pregnancy and lactation

ORS

May be used during pregnancy and lactation as there are no known adverse effects.
The safety of this product in human pregnancy has not been established.

ZINC TABLET

Zinc crosses the placenta and is present in breast milk.

4.7 Effects on ability to drive and operate machine

ORS

ORS could not be expected to affect the ability to drive or use machines.

ZINC TABLET

There is no evidence regarding the effect of zinc on the ability to drive or use machines, however
Zinc sulfate Tablet is not expected to have any effect on the ability to drive and use machines.

4.8 Undesirable effects

ORS

None stated

ZINC TABLET

Zinc supplementation is safe and effective. Zinc supplementation is found to have no long-term harm. Some children experienced vomiting and a slight decrease in copper status after consuming zinc.

4.9 Overdose

If significant over dosage occurs, serum and electrolytes should be evaluated.
Corrective measures should be carried out and levels monitored until a return to normal levels is achieved.

Symptoms

High doses of zinc cause emesis. In addition, zinc sulfate is corrosive at high doses, and may cause irritation and corrosion of the gastrointestinal tract, including ulceration of the stomach and possible perforation. Overdosage with zinc has also

been associated with acute renal tubular necrosis and interstitial nephritis. Prolonged high dose zinc supplementation may result in copper deficiency.
Treatment
In cases of acute zinc overdose, treatment is primarily supportive; however induced emesis, gastric lavage, or activated charcoal may be useful in cases of substantial ingestions of zinc tablets. Chelating agents such as calcium disodium EDTA may be useful.

5. Pharmacological properties

5.1 Pharmacodynamic properties

ORS

The product consists of physiological salts and glucose, which are used synergistically in solution to aid rehydration. The pharmacodynamic effect is to counter the drop in the extracellular fluid volume and electrolytes in mild to moderate diarrhoea.
Pharmacotherapeutic group: Other mineral supplements, ATC code: A12CB01

ZINC TABLET
Zinc sulfate is a zinc salt used for the treatment of acute and persistent diarrhoea in children.
Zinc is an essential trace element which is present in a wide range of foods. It is found in all tissues. Normal growth and tissue repair depend upon adequate zinc levels. Zinc acts as an integral part of several enzymes important to protein and carbohydrate metabolism. Severe zinc deficiency is associated with growth retardation, primary hypogonadism, skin disease, disturbances of taste and smell, and impaired immunity, with increased susceptibility to infection.
Zinc supplementation has been shown to reduce the duration and severity of diarrhea in populations of children with a high incidence of zinc deficiency, and also to reduce the frequency of recurrences in the subsequent 2-3 months. The beneficial effects of zinc are likely associated with reconstitution of the immune response, however direct inhibitory effects of zinc on enteric pathogens have also been reported.
ATC CODE: A12CB01

5.2 Pharmacokinetic properties

ORS

Sodium and glucose are actively transported via the membrane into the enterocytes. Sodium is then extruded into the intercellular spaces and the resulting osmotic gradient causes water and electrolytes to be drawn from the gut and then into the circulation.

ZINC TABLET

Absorption

Zinc is incompletely absorbed from the small bowel, with between 10 and 40% of an ingested dose absorbed. Numerous dietary components can interfere with zinc absorption, particularly phytates and fibre, which bind to zinc, resulting in poorly absorbed zinc complexes. The absorption of zinc was examined in 10 healthy, zinc replete, adult male volunteers (baseline mean plasma zinc level ±SD of 15.1 ±3.5 mmol/L). Absorption of zinc was rapid, with a maximal increase in mean plasma zinc level (±SD) of 11.6 (±6.0) mmol/L observed within approximately 2 hours of administration.

Distribution
Approximately 60% of circulating zinc is bound to albumin and roughly 30% is bound to macroglobulin. The majority of zinc is stored in the liver and kidney, chiefly intracellularly, and bound to metalloproteins.

Elimination
In adults, it has been estimated that approximately 0.5 to 1.0 mg/day is secreted in the biliary tract and excreted in the stool, while 0.5 to 0.8 mg/day is excreted in the urine.

5.3 Pre-clinical safety data

ORS/ ZINC TABLET

Non-clinical data have not revealed significant hazards for humans, based on standard studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and reproductive toxicity. Effects in non-clinical studies were observed only at exposures sufficiently in excess of the maximum human exposure to be of little clinical relevance.

6. Pharmaceutical particulars

6.1 List of excipients

ORS

ORS does not contain any excipient

ZINC TABLET
Zinc Sulfate contains below excipient:
Microcrystalline Cellulose BP
Lactose BP
Maize Starch BP
Croscarmellose Sodium BP
Povidone (PVPK-30) BP
Isopropyl Alcohol BP
Purified Talc BP
Sodium Starch Glycolate BP
Colloidal Anhydrous Silica (Aerosil) BP
Croscarmellose Sodium BP

Kyron T 314 BP
Flavour Orange IH
Aspartame BP
Magnesium Stearate BP

6.2 Incompatibilities

Not Applicable

6.3 Shelf-Life

36 months from the date of manufacture.

6.4 Special Precautions for Storage

Store below 30°C. Protect from light and moisture.

Keep medicine out of reach of children.

6.5 Nature and Contents of Container

20.5 gm powder packed in laminated sachet. 10 tablets to be packed in an Alu Pvc blister.

Such 2 sachets and 1 blister to be packed together in a carton along with pack insert.

6.6 Special precaution for disposal

ORS/ZINC TABLET

None stated.

7. Marketing authorisation holder

HALEWOOD LABORATORIES PVT. LTD.

Plot No. 319, Phase – II, G.I.D.C.,

Vatva, Ahmedabad – 382445.

8. Marketing authorisation number(s)

Not Applicable

9. Date of first authorisation/renewal of the authorisation

Not Applicable

10. Date of revision of the text

Not Applicable